

Abstract

The present invention provides a method of inhibiting the development of opioid tolerance using novel chimeric hybrid molecules containing an opioid moiety of chemically modified morphine (3) that binds to and activates the human mu (μ) opioid receptor, with the opioid moiety linked through a novel linker-hinge (4) to a substance P peptide fragment moiety (5) that binds to and activates the human substance P receptor. The hybrid alkaloid/peptide analgesics may be administered intrathecally, systemically or orally.